

Atty Docket No.: R0130D-CON
USSN: 10/823,012

REMARKS

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Claims 48 and 51-62 are pending in the above-identified patent application.

Claims 48 and 52 are amended herein. Claims 53-62 are withdrawn from consideration.

1. Declaration Under 37 CFR §1.132

The Examiner stated that the Declaration filed on May 10 2006 by Counde O-Yang is insufficient to overcome the rejection because: (1) the showing is directed to, or relying on, blood pressure changes only and not treating incontinence; (2) the various representative points (squares, triangles, circles) on the graphs of Figures 1 and 2 were not distinguishable or legible; and (3) the showing was not commensurate in scope with the claimed invention. Applicants address each of these points below.

a. Showing Directed To Blood Pressure Changes Only And Not Treatment Of Incontinence

The Examiner stated that "the showing is directed to, or relying on, blood pressure changes only and not treating incontinence". The Applicants respectfully disagree. Applicants specification and Rule 1.132 Declaration disclose data directly related to treatment of incontinence, in addition to blood pressure data.

Alpha 1A agonists are known to increase muscle tone in the lower urinary tract (p. 1 lines 19-20 of Applicants' specification). Activation of alpha 1A adrenoceptors located on the smooth muscle cells of the proximal urethra and bladder neck evokes contraction and an increase in urethral closure pressure (p. 2 lines 10-12). The retentive pressure or tension of the urethral sphincter is known in the art as "intraurethral pressure" or IUP. "Intraurethral pressure" or IUP is the retentive pressure of the urethral sphincter, and not a form of blood pressure. Increasing IUP by administration of alpha 1A agonists can prevent involuntary loss of urine. The most common manner of *in vivo* testing of drugs for treatment of incontinence is to measure effect on IUP in various animal models. Applicants have measured IUP using an anesthetized rabbit model using transducer measurement of IUP (p. 32 lines 09-14, p. 58 line 20 through p. 59 line 16).

Applicants' Rule 1.132 Declaration directly provides intraurethral pressure data, which is indicative of ability to prevent involuntary urine loss as noted above.

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Accordingly, Applicants respectfully submit that the Examiner cannot reasonably conclude that Applicants' Declaration discloses only blood pressure data.

As previously noted by Applicants, an undesirable side effect of alpha 1A agonists is increased blood pressure, which can occur concurrently with an increase in IUP following administration of alpha 1A agonists. Blood pressure is typically measured as mean arterial pressure or "MAP" (p. 32 lines 12-14, p. 59 lines 5-7) by positioning a telemetry receiver adjacent to the test animal in a conventional manner. Compounds that result in an increase in mean arterial blood pressure (MAP) concurrently with an increase in intraurethral pressure (IUP) are not attractive drug candidates. The ability to increase IUP while avoiding increase in MAP is known as "uroselectivity", and is a desirable property for alpha 1A agonists (see, e.g., paragraph 2 of Applicants' Declaration).

b. Representative Points On Graphs Not Distinguishable

The Examiner stated that the various representative points (squares, triangles, circles) on the graphs of Figures 1 and 2 were not distinguishable or legible. Applicants have reproduced Figure 1 and Figure 2 below in expanded form so that the representative points can be more clearly seen.

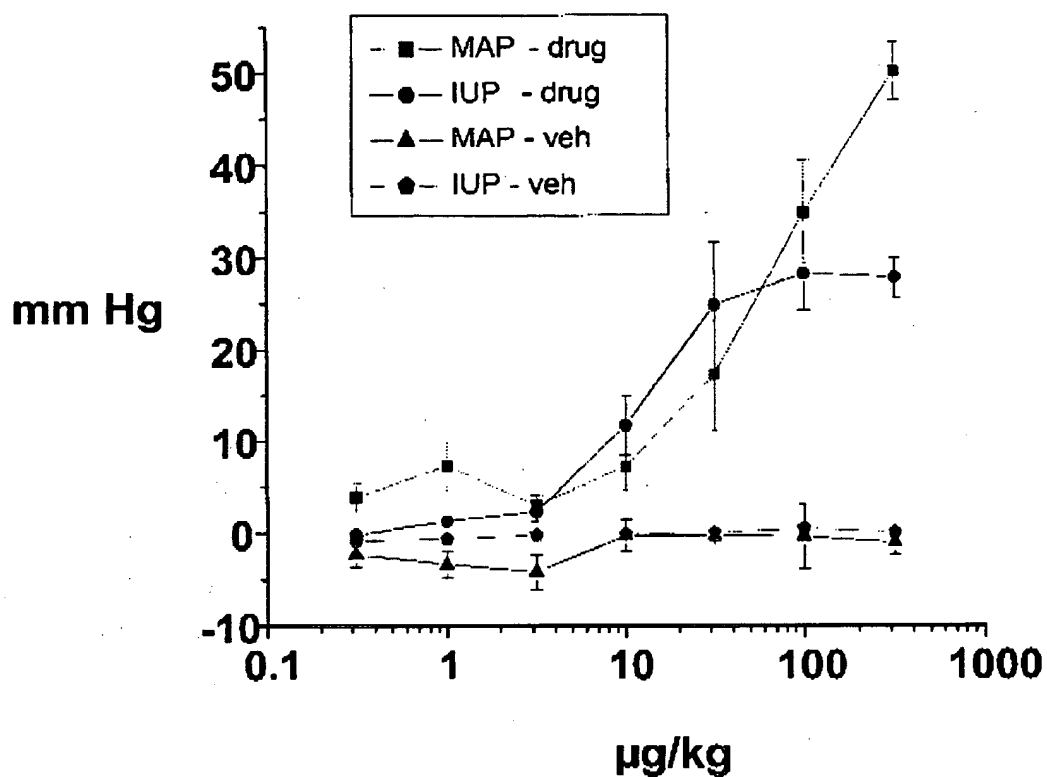
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Figure 1.

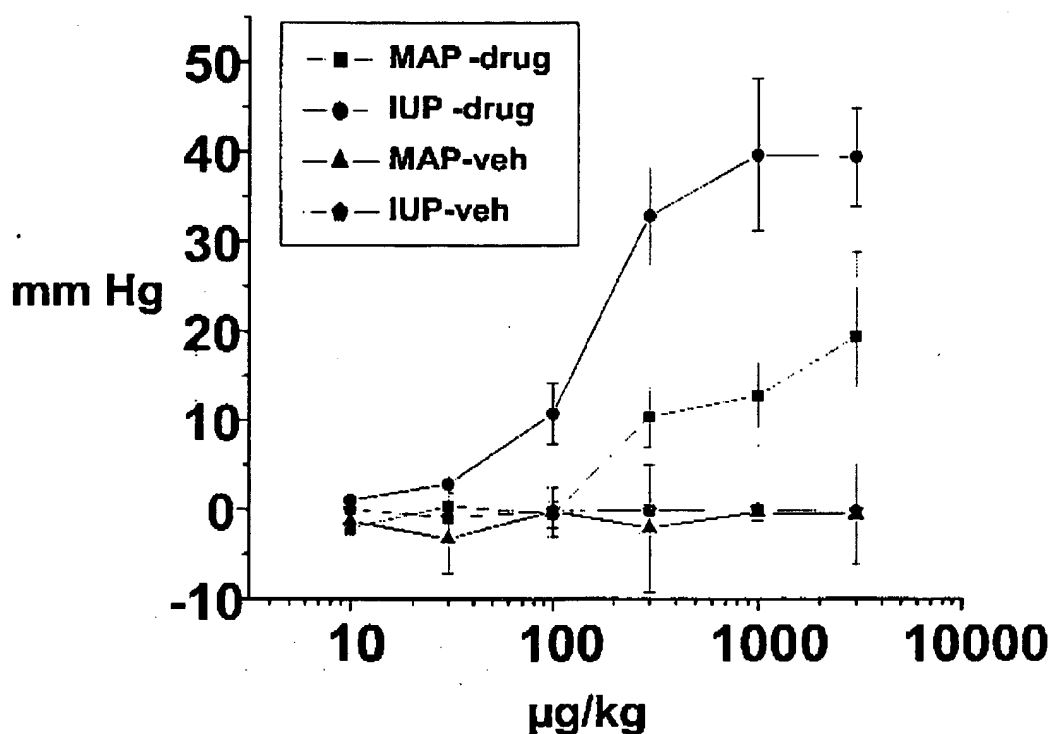
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Figure 2.

c. Showing Not Commensurate In Scope With Claimed Invention

The Examiner stated that the showing of Applicants' Rule 1.132 Declaration was not commensurate in scope with the claimed invention. A table of compounds was provided by the Examiner to illustrate additional compounds for which persuasive comparison data could be made.

Applicants unfortunately do not have any additional comparison data. Applicants have amended base claim 48 to narrow its scope to $R^1 = \text{methyl}$ and $R^4 = \text{methyl; fluoro; chloro; bromo; hydroxy; methoxy; or ethoxy}$. Claim 52 has been amended to conform to amended claim 48. Applicants' claims cover only seven specific compounds having a similar substitution pattern. Applicants respectfully believe that the showing of the Rule 1.132 Declaration is now commensurate in scope with Applicants claims.

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2. Double Patenting

Claims 48-52 and 54 were rejected under the judicially created doctrine of Obviousness-type double patenting in view of Cournoyer et al., which discloses positional isomers (*meta* versus *para*) of the instantly claimed compounds.

As previously noted, Applicants' Declaration under 37 CFR §1.132 demonstrates unexpectedly better ability of the claimed compounds to increase IUP without causing an undesirable increase in blood pressure, compared to the compounds of Cournoyer et al. In view of the further remarks above, and the amendment made to claims 48 and 52, Applicants believe claims 48-52 and 54 are now patentably distinct from the teachings of Cournoyer et al.

2. Rejection Under 35 USC §103

Claims 48-52 and 54 were rejected under 35 USC §103 as unpatentable over Cournoyer et al., US 5,952,362, which discloses and claims structural isomers (*meta* versus *para*) of the compounds claimed in the above-identified application.

As pointed out above, Applicants' Declaration under 37 CFR §1.132 demonstrates unexpectedly better ability of the claimed compounds to increase IUP without causing an undesirable increase in blood pressure, compared to the compounds of Cournoyer et al. In view of the further remarks above, and the amendment made to claims 48 and 52, Applicants believe claims 48-52 and 54 are now patentably distinct from the teachings of Cournoyer et al.

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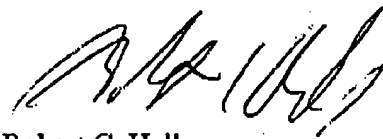
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CONCLUSION

In view of the foregoing, Applicants believe that the pending claims in the above identified patent application are patentable over the prior art of record and in condition for allowance. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-354-7540.

Please charge the fee for a three month Extension of time (37 C.F.R. §§ 1.17(a)(3)) to Deposit Account No. 18-1700.

Respectfully submitted,



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